Incidence of cancer among grand multiparous women in Finland with special focus on non-gynaecological cancers : A population-based cohort study

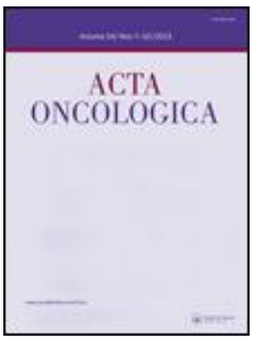
Högnäs, Emma

2016-03-03

Högnäs , E , Kauppila , A , Hinkula , M , Tapanainen , J S & Pukkala , E 2016 , ' Incidence of cancer among grand multiparous women in Finland with special focus on non-gynaecological cancers : A population-based cohort study ' , Acta Oncologica , vol. 55 , no. 3 , pp. 370-376 . https://doi.org/10.3109/0284186X.2015.1063775

http://hdl.handle.net/10138/223902
https://doi.org/10.3109/0284186X.2015.1063775

publishedVersion



Taylor & Francis
Taylor & Francis Group

Acta Oncologica, 2016; 55: 370 376

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Incidence of cancer among grand multiparous women in Finland with special focus on non-gynaecological cancers: A population-based cohort study

EMMA HÖGN˜S[1], ANTTI KAUPPILA[2], MARIANNE HINKULA[2], JUHA S. TAPANAINEN[1,2] & EERO PUKKALA[3,4]

[1]Department of Obstetrics and Gynaecology, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland, [2]Department of Obstetrics and Gynaecology, Medical Research Center Oulu, Oulu University Hospital, Oulu, Finland, [3]Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland and [4]School of Health Sciences, University of Tampere, Tampere, Finland

ABSTRACT

Background. Many studies have previously revealed evidence of an association between grand multiparity (ve or more deliveries) and gynaecological cancer. Oestrogen has an impact on cancer formation and the amount of circulating oestrogen is signi cantly higher during pregnancy. Also the lifestyle of grand multiparous women differs somewhat from the average population. Considering these factors it is plausible that also non-gynaecological cancers are associated with multiparity. The aim of our study was to determine cancer incidence among grand multiparous women, with special attention to non-gynaecological cancers.

Material and methods. All 102 541 women alive in 1974 2011 and having had at least ve deliveries were identi ed in the Finnish Population Register and followed up for cancer incidence through the Finnish Cancer Registry to the end of 2011. Standardised incidence ratios (SIRs) were de ned as ratios between observed and expected numbers of cases, the latter ones based on incidence in the entire Finnish female population.

Results. The overall incidence of non-gynaecological cancers was the same as in the reference population (SIR 0.98, 95% con dence interval 0.90 1.06). The incidence of cancers of the gall-bladder (SIR 1.42, 1.26 1.58), biliary tract (1.19, 1.04 1.35) and kidney (1.22, 1.14 1.31) was increased. There were signi cantly fewer cases than expected of urinary bladder cancer (SIR 0.70, 0.61 0.78), lung cancer (0.87, 0.81 0.92), colon cancer (0.94, 0.89 0.99) and all types of skin cancers. As a consequence of the decreased incidence of gynaecological cancers (SIR 0.74, 0.71 0.77) and breast cancer (0.60, 0.58 0.61), the SIR for cancer overall was 0.84 (0.83 0.85).

Conclusion. The study demonstrated that grand multiparous women have a similar overall risk of non-gynaecological cancers as other women, despite signi cant differences in some speci c forms of cancer.

A multitude of studies have previously revealed strong evidence of an association between grand multiparity (ve or more deliveries) and gynaecological cancer. Grand multiparous (GM) women are known to have decreased incidence of endometrial, ovarian and breast cancer, while the incidence of cervical cancer may be increased [1 4]. Pregnancies and breast feeding periods are a dominant part of the reproductive life of GM women, who therefore differ markedly from other women as regards lifestyle and hormonal environment. Oestrogen receptors are widely distributed in mammalian tissues and present the rst step in a pathway where oestrogen affects malignant transformation, i.e. through DNA damage [5]. New evidence further shows that oestrogen has an impact on carcinogenesis in general [6], and also speci cally, i.e. colon, thyroid and lung cancer have been shown to be in uenced by sex steroids [7 9].

The risk of cancer is greatly dependent on lifestyle factors, which may in many ways be different in

This study is one of the largest ever done on cancer incidence among grand multiparous women and provides valuable information about the effects of multiple pregnancies on women s cancer risk.

Correspondence: E. Pukkala, Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Unioninkatu 22, 00130 Helsinki, Finland. Tel: 358 50 3002413. E-mail: eero.pukkala@cancer.

(Received 25 February 2015; accepted 10 June 2015)

ISSN 0284-186X print/ISSN 1651-226X online ' 2015 Informa Healthcare
DOI: 10.3109/0284186X.2015.1063775

multiparous and other women. For instance, mortality from ischaemic heart disease and diabetes appears to be elevated among Finnish GM women [1 4,10]. Nevertheless, the incidence of non-gynaecological cancers in GM women has not been studied to a great extent. The ndings on risks of non-gynaecological cancers are not consistent but there are scattered observations on signi cantly decreased or increased incidence of several cancer types. For example, a Taiwanese study observed [7] 28% decreased risk for colon cancer among women with four or more deliveries as compared to women with only one delivery, while a recent Egyptian study observed an odds ratio (OR) as low as 0.3 (0.1 0.5) for colorectal cancer among women with seven reported pregnancies compared with women who reported 1 3 deliveries [11]. In a meta-analysis by Dietrich et al. [12] the risk for bladder cancer among ever parous women was one third lower than among nulliparous women, and the OR for GM women was 0.74, although with a rather wide CI (0.35 1.57). In a Chinese study [13] the risk for gall bladder cancer was increased for women with ve deliveries as compared with women with one delivery (OR 2.20, 95% CI 1.01 4.66). In a cohort study by Kabat et al. the risk for renal cancer increased with increasing parity and HR for GM women was 2.41 (95% CI 1.27 4.59) compared to nulliparous women [14].

The aim of this study was to obtain more information on the long-term risks and bene ts of multiple pregnancies. A secondary aim was to update the results related to gynaecological cancers among the Finnish GM population reported about 10 years ago [1 4].

Material and methods

The study cohort consisted of all Finnish women having their fth child before 2011, and who had not emigrated or died before 1974. The cohort was drawn from the Finnish Population Register, and consisted of 104 896 women. Those born abroad (n 2355) were excluded because the data on their parity history may be unclear. Thus the nal size of the cohort was 102 541 women.

For calculation of person-years of follow-up the starting point was 1 January 1974 or birth of the fth child, whichever came later, and the end-point was the date of emigration or death, or 31 December 2011, whichever occurred rst. The total number for person-years of follow-up was 2 672 587 (Table I). The follow-up could not start before 1974 because the mother-child links in the Finnish population register were not created if the mother had died before October 1973.

Information on cancer cases in the cohort was obtained from the national population-based Finnish Cancer Registry, using record linkage based on personal identity codes. The cancer cases were classi ed according to the main topographic categories, using the ICD-10 classi cation system (Table II).

Table I. Number of women (N) and person-years in the GM-cohort in each age group, follow-up period and listed according to age at rst birth. The numbers in N column refer to the age in the beginning of follow-up. The respective numbers of person-years refer to the dynamic age during follow-up (i.e. a woman may contribute person-years to several categories).

	years	N	Person-years
Age at follow-up	20 29	8 940	19 140
	30 39	35 134	217 805
	40 49	34 556	493 342
	50 59	21 296	667 342
	60 69	2 614	645 106
	70 79	1	459 789
	80		170 063
Time since fth delivery	0 4.99	42 201	180 921
	5 9.99	14 276	201 152
	10	46 064	2 290 513
Age at rst birth	20	20 364	518 453
	20 25	53 264	1 421 398
	26 29	22 961	591 576
	30	5 952	141 160

The expected numbers of each cancer type were calculated by multiplying the number of person-years of the GM women in each ve-year age category and calendar period (1974 1980, 1981 1987, 1988 1993, 1994 1999, 2000 2005, 2006 2011) by the cancer incidence rate among all Finnish women in the same age and calendar time category. SIRs were de ned as the ratios between the observed and expected numbers of cases. Con dence intervals (CIs) for the SIRs were based on the Poisson distribution of the observed number of cases. The analyses were further strati ed according to age at follow-up (20 29 years, 30 39 years, 40 49 years, 50 59 years, 60 69 years, 70 79 years and 80 years or older) age at rst birth (20 years, 20 24 years, 24 30 years and 30 years or older) and time since fth birth (0 4.99 years, 5 9.99 years and 10 years or longer).

Results

During the follow-up period 16 322 cancers were diagnosed in the GM cohort.

Of the non-gynaecological cancers (Table II), signi cantly decreased SIRs were observed for lung cancer (SIR 0.87, 95% CI 0.81 0.92), bladder cancer (SIR 0.70, 95% CI 0.61 0.78) and cancer of unknown origin (0.62, 95% CI 0.55 0.68). The rates for all types of skin cancer were also signi cantly decreased. The risk of skin melanoma was especially low during the rst 10 years after the fth birth (SIR 0.38, 95% CI 0.21 0.63).

Table II. Observed (OBS) and expected (EXP) numbers of non-gynaecological cancer cases, and standardized incidence ratios (SIR) with 95% con dence intervals (CI), among grand multiparous women in Finland 1974 2011, by site.

ICD-10	Site	OBS	EXP	SIR	95% CI
	All sites	16 322	19 417	0.84	0.83 0.85
	All sites, excluding breast cancer and gynaecological cancers	11 144	11 402	0.98	0.90 1.06
C00	Lip	70	66	1.07	0.83 1.35
C01 02	Tongue	55	70	0.79	0.59 1.02
C03 06	Mouth, other	73	73	1.00	0.78 1.25
C07 08	Salivary glands	41	42	0.97	0.69 1.31
C09 14	Pharynx	30	36	0.82	0.56 1.17
C15	Oesophagus	147	162	0.91	0.77 1.06
C16	Stomach	746	731	1.02	0.95 1.09
C17	Small intestine	69	63	1.10	0.85 1.39
C18	Colon	1180	1257	0.94	0.89 0.99
C19 21	Rectum, rectosigmoid, anus	684	713	0.96	0.89 1.03
C22 24	Liver, gallbladder and biliary tract	696	563	1.24	1.06 1.42
	Liver	183	172	1.06	0.91 1.22
	Gallbladder	294	207	1.42	1.26 1.58
	Intra- and extrahepatic bile ducts	219	184	1.19	1.04 1.35
C25	Pancreas	830	809	1.03	0.96 1.09
C26	Other digestive organs	71	65	1.09	0.85 1.37
C30 31	Nose, sinuses	29	30	0.96	0.65 1.38
C32	Larynx, epiglottis	32	26	1.23	0.84 1.73
C33 34	Lung, trachea	888	1019	0.87	0.81 0.92
C40 41	Bone	21	21	1.02	0.63 1.55
C43	Skin melanoma	395	527	0.75	0.68 0.82
C44	Skin, squamous cell carcinoma	647	721	0.90	0.83 0.96
C45	Mesothelioma	29	37	0.78	0.52 1.11
C46	Kaposi sarcoma	7	10	0.68	0.27 1.40
C47	Autonomic nervous system	2	5	0.38	0.04 1.32
C48 49	Soft tissues	124	127	0.98	0.81 1.15
C64 65	Kidney	781	638	1.22	1.14 1.31
C66 68	Bladder, ureter, urethra	244	349	0.70	0.61 0.78
C69	Eye	52	51	1.06	0.80 1.38
C70 72, D32 33, D42 43	Brain, central nervous system	702	751	0.93	0.87 1.00
C73	Thyroid gland	436	334	1.31	1.19 1.43
C74 75	Other endocrine glands	25	18	1.37	0.88 2.01
C76, C80	Cancer of unknown origin	354	574	0.62	0.55 0.68
C81	Hodgkin lymphoma	48	56	0.86	0.63 1.13
C82 85, C96	Non-Hodgkin lymphoma	708	727	0.97	0.90 1.04
C90	Myeloma	315	299	1.05	0.94 1.17
C91 95	Leukaemia	394	399	0.99	0.89 1.08
	Not included above				
	Basal cell carcinoma of the skin	4120	5048	0.82	0.79 0.84

Signi cantly increased SIRs were observed as regards cancer of the gall-bladder (SIR 1.42, 95% CI 1.26 1.58), extra- and intrahepatic bile ducts (SIR 1.19, 95% CI 1.04 1.35), kidney (SIR 1.22, 95% CI 1.14 1.31) and thyroid gland (SIR 1.31, 95% CI 1.19 1.43).

The incidences of breast cancer, endometrial cancer and ovarian cancer were markedly decreased, while that of cervical cancer was increased (Table III). Among lesions registered by the Finnish Cancer Registry but not regarded as cancers, the SIRs for in situ lesions of breast cancer and borderline tumours of the ovary were signi cantly below 1.0 and the SIR for precursor lesions of cervical cancers was signi - cantly above 1.0. The SIRs increased with increasing age at follow-up. For instance, the SIRs in age category 80 years were 0.69 (95% CI 0.62 0.76) for breast cancer, 0.80 (95% CI 0.65 0.96) for endometrial cancer, 0.85 (95% CI 0.67 1.07) for ovarian cancer and 1.45 (95% CI 1.00 2.03) for cervical cancer. The SIR for cervical cancer according to age at follow-up followed a U-shaped curve, with the lowest SIR (1.02, 0.81 1.26) in age category 60 69 years.

As regards most cancers there was no signi cant variation in SIRs according to age at rst birth, time of follow-up since fth birth and age at follow-up, a few exceptions were nevertheless noted. The SIR for renal cancer was high among women with low or high age at rst birth (Figure 1). Similar pattern for

Table III. Observed (OBS) and expected (EXP) numbers of breast cancer and gynaecological cancer cases, and standardized incidence ratios (SIR) with 95% con dence intervals.

ICD 10	Site	OBS	EXP	SIR	95% CI
C50	Breast	3137	5265	0.60	0.58 0.61
C51 57	Gynaecological cancers	2041	2751	0.74	0.71 0.77
C53	Cervix	356	289	1.23	1.11 1.36
C54	Endometrium	864	1352	0.63	0.58 0.66
C55	Uterus, other	23	27	0.86	0.55 1.29
C56	Ovary	594	847	0.70	0.65 0.75
C51 52, C57	Other female genitals	222	235	0.95	0.83 1.07
Premalignant lesions:					
	Breast; carcinoma in situ	113	220	0.51	0.42 0.61
	Cervix cancer; precursor	419	354	1.18	1.07 1.30
	Ovary, borderline tumour	114	148	0.77	0.64 0.91

SIRs according to age at rst birth was not seen in any other cancer form. Concerning stomach cancer, the overall incidence in the cohort was similar to that in the reference population, but there was a peculiarly very low risk in the follow-up period of 5 9.99 years after the fth birth, with only one case observed versus 11.1 expected (SIR 0.09, 95% CI 0.00 0.49). In turn, a four-fold statistically signi cant increase in the incidence of multiple myeloma was seen during the rst ve-year follow-up period after the fth birth, based, however, on only four observed cases (SIR 4.41, 95% CI 1.20 11.28), while the incidence of myeloma among GM women in later follow-up was close to that in the reference population.

Discussion

The total incidence of non-gynaecological cancer was virtually the same as in the reference population.

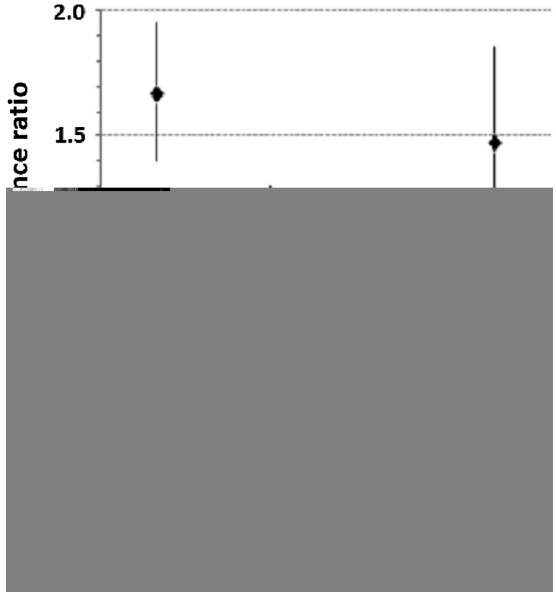


Figure 1. Standardized incidence ratio (SIR) of renal cancer, with 95% con dence intervals, according to age at rst birth.

However, the incidence of some cancer types among GM women was signi cantly different compared with that in Finnish women in general. A decreased SIR was observed in cancers of the lung, bladder and skin, increased SIRs for kidney, thyroid, bile duct and gall-bladder. The total cancer incidence was decreased, mostly because of a decreased incidence of all gynaecological cancers and breast cancer.

This study is one of the largest GM women study ever done. It was conducted in a country with registers containing reliable data on births and cancer diagnoses. The personal identity codes given to every Finn since 1967 guarantee accurate record linkage. The reporting and diagnostic praxis is virtually the same everywhere in Finland. As we only had indirect information on lifestyle factors, our possibilities to evaluate the potential effects of confounders are incomplete.

A large part of the GM cohort belongs to the Laestadian movement within the Lutheran church in Finland, which is especially common in the northern parts of the country. Among members of the Laestadian movement the use of contraceptives is strictly forbidden, alcohol consumption is rare, but smoking is permitted. Grand multiparous women are more likely to be married than women in the reference population, and the income of Finnish GM families may be satisfactory, as an allowance is paid by the state for each child [15]. Multiple pregnancies are associated with signi cant weight gain followed by obesity and increased mortality from type II diabetes mellitus [10,16].

Smoking was predicted to cause 82% of all lung cancers, 25% of bladder cancers and 7% of kidney cancers of Finnish women in 2000 [17]. The low SIR for lung cancer (0.86) in this cohort ts with the fact that smoking among Finnish GM women is less frequent than among other women [18]. Although there is one observation of a decreased incidence of lung cancer among non-smoking GM women (hazard ratio 0.50, 95% CI 0.28 0.88) compared with non-smoking women with one or two children [9,19], it